

Wexler ↓

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DEPARTMENT OF PSYCHIATRY

722 West 168th Street

October 20, 1990

Professor Joshua Lederberg
President Emeritus
1230 York Avenue
New York, NY. 10021-6399

Dear Joshua,

Thanks for sending me your epistle on privacy. I hope that The Scientist publishes it. You do an excellent job in laying out the dilemmas of insurance agencies as well as those who use genetic clairvoyance to alter insurance calculations for the future. The actuaries stack the decks according to certain calculations of what it takes for them to make money. The idea of independent cowboy operators shuffling these decks and restacking them in their favor is troubling to the insurance industry. On the other hand, as you say, we can't refuse to give out the information because the insurance agencies won't like it and there are grave risks in sharing such private data as well. Insurance companies even now will not insure people at risk for Huntington's disease - if they know about it - and are not likely to be sympathetic to gloomy news. Perhaps there should be some kind of "no fault" insurance with a relatively easy to obtain minimum coverage and more stringent requirements for additional amounts of protection.

I am curious about your interest in the mitochondrial paper. There has been a recent flurry of interest in the mitochondria of patients with Huntington's disease and even some preliminary findings of mitochondrial deletions. When the enclosed mitochondrial paper was written, Carol Irwin and Jim Gusella were looking primarily for mitochondrial polymorphisms which would segregate with the appearance of juvenile Huntington's disease. Although they did not notice any obvious mitochondrial deletions, they did not look at the entire mitochondrial genome.

The hypothesis we were exploring was that a mitochondrial factor may be protective against early onset Huntington's disease. There is a selective advantage in having this mitochondrial factor, according to this hypothesis, so that women tend to keep and pass on mitochondria predisposing toward adult onset. The offspring of males would have the mitochondria of women marrying into the Huntington's disease population, who may

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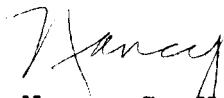
or may not have this protective factor. This would account for the fact that the vast majority of children manifesting with juvenile Huntington's disease are born to affected fathers.

In Venezuela, due to the fact that there was a founder mother and many females throughout the pedigree, all the patients in a particular branch, both with adult and juvenile onset Huntington's disease, have the same mitochondria. The hypothesis was not supported.

There is now interesting research proceeding at Johns Hopkins and Columbia Universities suggesting that there are mitochondrial deletions in Huntington's disease brain tissue. These deletions do not appear to be unique to Huntington's disease, and can be found in Parkinson's disease and perhaps other diseases of aging as well. The Hereditary Disease Foundation is trying to get a better understanding through an upcoming workshop of the exact nature of these deletions and what their functional impact might be. Many Huntington's patients seem to have metabolic difficulties requiring enormous amounts of calories to maintain a steady weight. This may be due to the monumental caloric requirement generated by constant choreic movements but there may also be some metabolic flaw more intrinsic to the gene lesion itself.

I would be happy to answer any questions you might have.

Sincerely,

A handwritten signature in cursive script, appearing to read "Nancy".

Nancy S. Wexler
Associate Professor
Clinical Neuropsychology